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IRBs grappling with tissue requests from biotech firms

Informed consent is an issue

Technology advances have driven increased interest in molecular studies involving tissue analyses. As a result, biotech firms increasingly are asking scientists to sell human tissues for study by outside enterprises.

This trend has come to the Thomas Jefferson University IRB's attention in recent years, says **J. Bruce Smith**, MD, CIP, director of the office of human research and division of human subjects protection at Thomas Jefferson University in Philadelphia.

"There's a big push to get these studies done, and it's increased," Smith adds.

Since the financial and federal budget crises have made research funding scarcer, academic researchers have been looking for alternative funding sources for their labs. The biotech firms' offers have appealed to them, says **Kyle Conner**, MA, CIP, associate director of the division of human subjects protection at Thomas Jefferson University.

"All investigators are looking for ways to generate money," Conner adds. "We say, 'It's okay to get paid, but it has to be a scholarly pursuit.'"

Smith, Conner, and other Thomas Jefferson University officials began to discuss this trend at a meeting when an investigator asked if he could provide tissue to a company that would send it to another company for research.

"We were concerned because it didn't seem like an ethical thing to do," Smith says.

After discussions with the IRB and institutional leaders, they decided on an ethical approach that is outlined in the institution's tissue policy and a tissue consent form, he adds.

"We developed a consent form to allow people to bank anonymized tissue for future research," Smith says. "Also the policy and consent form state that we would not sell their tissue for profit."

If researchers are approached about sending tissue to other research

facilities, they are permitted to do so only if the researcher meets criteria for having a scholarly or academic interest in the research.

"The motivation for creating these forms was to address studies comprised exclusively of tissue collection," Conner says. "We don't want investigators to fill out forms they don't need, and a lot of tissue studies don't need to include informed consent."

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Editorial Questions

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A number of academic medical centers have developed similar policies in recent years because they also have been confronted with the business of selling tissue, Smith notes.

"We all want our investigators to have some sort of scholarly or academic interest in this," he says.

Human tissue for study increasingly will be in demand as scientific advances open up research possibilities, but IRBs and academic research institutions have a responsibility to be accountable to the public interest and perceptions, Smith and Conner say.

"Academic medical centers have to be concerned with their reputations," Conner says.

"It's not our main concern, but it is a concern of our office; we don't want lurid headlines to appear in the paper about selling tissue for profit," he adds. "We want to keep the community enthusiastic for research."

Complex informed consent issues

While for-profit sale and use of human tissue might bother some people, the bigger issue is informed consent, says **Marshall B. Kapp**, JD, MPH, director of the Center for Innovative Collaboration in Medicine and Law at Florida State University in Tallahassee.

Kapp also is a professor in the college of medicine and college of law.

"Does that person giving consent know that their tissue is going to be used for research generally, and do they know the specific kinds of research in which their tissue will be used?" Kapp says.

"I don't have an objection to selling tissue to a commercial entity to do research if the human being from whom the tissue was taken knows about that and consents to it," he adds.

Ideally, each person who has provided specimens being stored at a medical research facility would be contacted by the university or another group about providing informed consent for any and all uses of their tissue, Kapp says.

Obtaining consent in this way is impractical, if not impossible, he acknowledges.

"So the open-ended consent might be a good compromise, but it should say something about the possibility that the tissue sample will be transferred to the for-profit entity for research purposes," Kapp says. "People won't know what kind of specific research project will be

involved, but they at least will know about the possibility."

Thomas Jefferson University's IRB follows federal regulations regarding waivers of informed consent for stored tissue, Conner says.

"With any prospective collection of tissue we would require informed consent and have an informed consent template," he says. "If the tissue already is stored, we may waive consent because the subjects are no longer available, and it's not really practical to obtain consent for tissue that's already stored."

The IRB has seen different types of consent approaches, including forms that are very general with open-ended consent and those that give people the opportunity to check a box or specify which types of research they would like their tissue to be used for, he adds.

"We would like the consent to be as specific as possible, but in a lot of cases they don't know what the tissue will be used for, so we have them explain what they do know: They're going to put the specimen in a tissue bank at this location, it will be stored for x number of years, and the subject can withdraw the tissue," Conner says.

Contract agreements

Thomas Jefferson University's OHR 15 form, recently revised, reflects a contract in which a company that has interest in a biological specimen sends money to the university or medical college for the tissue.

"The contractual agreement between the company and university says this investigator will collect data that's generated, help with writing a manuscript, help analyze and be part of the team that writes the manuscript for publication," Smith says. "These are the sorts of things we feel would constitute a scholarly activity on the part of our faculty, and that's what we ask them to confirm on the form."

Since forming the new policy, the institution has seen a modest increase in researchers participating in studies involving biological specimens, he adds.

After making the change to require investigators to engage in scholarly activity, the IRB notified the research community of the change in its newsletter and through emails, Smith says.

"We had some push back from a couple of people who didn't understand it, who didn't get the concept of scholarly activity, but by and large it's been accepted by most researchers," he adds.

The informed consent and biological specimen issue is more complex.

Some ethicists and others do not believe the blanket consent is enough for stored biological specimens, Kapp notes.

"They believe true consent relies on enough information about the particulars of the research protocol to make it more meaningful," he says.

This concern is not based on the potential of harm because in the case of research involving tissue samples, the only risk is the breach of confidentiality, Kapp says.

"However, you have to look at autonomy more broadly," he explains. "I might say, as the source of tissue, that I don't philosophically or religiously want my tissue used for certain purposes even if there's no risk to me other than offending my moral principles." ■

Dust off those checklists, tools, templates

IRBs offer improvement ideas

As IRB offices gear up for a busy academic research year, it's a good idea to dust off IRB templates, checklists, and other tools to revise, improve, and adapt to technology and other changes.

IRBs need to review their templates and forms at least once a year, making changes when suggested by research teams and others, says **Kathryn G. Schuff**, MD, MCR, professor and chair of the IRB at Oregon Health & Science University in Portland.

"We update our consent form once or twice a year," Schuff says. "We do this when we have input from our research team about parts of consent that work well or don't work as well as a tool for the consent process. We consider feedback when tweaking the consent template itself and sharing tips that come from a research team."

IRB Advisor asked Schuff and other directors of IRB, research compliance, and human subjects protection offices nationwide to share some of their experiences and tips about improving IRB forms and templates. Here is their

advice about creating new forms and modifying different ones.

Updated consent templates

After the HIPAA rule modifications, published in the *Federal Register* on Jan. 25, 2013, research sites were permitted to use a single authorization form for compound authorizations containing conditioned and unconditioned authorizations of personal health information related to research activities. The 2013 rule change modified exceptions for using informed consent and disclosures on the same form, Schuff notes.

After this change, the Oregon Health & Science University IRB changed its clinical research consent summary to incorporate all HIPAA-required elements, she says.

For example, to satisfy the HIPAA authorization core element of an individual's right to revoke his or her authorization, the informed consent form states, "If you do join the study and later change your mind, you have the right to quit at any time. This includes the right to withdraw your authorization to use and disclose your health information."

The informed consent form has always had information about protecting research subjects' privacy and confidentiality, and the separate HIPAA form was a duplication of that information, Schuff says.

"We used the required elements of an authorization and found places in the informed consent where they fit well with the required elements of the informed consent document," she explains. "We spent a lot of time trying to make it sound less legalistic and more conversational and understandable to subjects."

The resulting form had the HIPAA elements so seamlessly woven into the IC required elements that some IRB members were concerned that the IC form did not adequately address HIPAA, she notes.

"We had to explain that it was an integrated form, and we offered IRB members an informed consent template with each of the HIPAA elements highlighted and with comments about the particular authorization," she says.

The change pleased research teams, Schuff says.

"Our feedback shows that it makes more sense to subjects to just talk about HIPAA and informed consent once and have them put together [on one form]," she says. "There also is less risk of having missing signatures on the HIPAA authorization."

Case study research chart/record review

Medical students on rotation often conduct chart reviews or case study reports as part of their professional development, says **Brian A. Gladue**, PhD, CIP, executive director for the office of research compliance at the University of North Texas Health Science Center in Fort Worth.

"We wanted to provide a process for them to think through and address the issues related to activity involving a patient's case record," he says.

"In many institutions this kind of research project would be exempt from IRB review, and most of the time it is exempt, particularly if information/research data that identify the individual subject are not recorded," he adds.

The institution needed a form that students or investigators could use to record information necessary for the IRB to approve the exempt status. With all the elements in place, the IRB could log it in as an exempt category review, Gladue says.

Before developing the form, investigators had to write a full protocol or multiple pages of documentation.

"Sometimes people inexperienced with research activities were not sure which information was relevant, so we wanted to standardize the thinking process students would need when conducting a chart review or when dealing with a single subject report," Gladue explains.

The resulting one-page form asks for basic protocol information, including the project's title, principal investigator's name, department, phone number, email, key personnel, and a brief description of the case study research project.

It lists these six criteria that must be met in order for the case study project to be approved as exempt:

- The case study research will involve a review of existing medical charts, clinical care charts, and/or records that have been generated as a matter of "standard of care."
- The case study will involve records for one patient.
- Patient data will be de-identified and protected under confidentiality requirements.
- All students, staff, and faculty involved in the case study must have completed appropriate human subjects research training (such as CITI).
- Only UNTHSC-affiliated institutions, hos-

pitals, clinics, sites, and practices where medical and/or clinical records will be maintained and assessed will be involved in the case study.

- The case study will only involve the analysis and reporting of existing information (a so-called "retrospective study"). Analysis of information not yet in the medical chart and/or record is considered a "prospective" review/study and is not allowed under this procedure.

The form is then signed and certified by the investigator and co-investigators.

Even with a short form, students and investigators sometimes make mistakes or give too little information about the proposed case study, Gladue notes.

IRB Record/Chart Review/Database form

The HIPAA rule and all changes, including the Health Information Technology for Economic and Clinical Health (HITECH) Act, could be reflected in a wide range of IRB templates and forms.

For example, forms might add language pertaining to unique health identifiers, according to **J. Bruce Smith**, MD, CIP, director, office of human research and division of human subjects protection at Thomas Jefferson University in Philadelphia.

Thomas Jefferson University's IRB addresses HIPAA in its record/chart review/computer database research study form with specific questions about how data will be used, including these:

- How many subject or database records will be reviewed?
- Will data be sent outside of TJU?
- If yes, where will data be sent?
- Why is it necessary to send data outside of TJU?
- How will data be sent? (Describe actual methods and include plans for coding and/or encryption.)
- Data to be used for: publication, oral presentation, other?
- Please check all categories of data that will be obtained during the record/database review: demographics, diagnosis, lab values, clinic notes, billing/charges, location of service, drug/device utilized, length of stay, radiology testing, procedures/treatment, provider of record who saw patient and signed discharge note, other?

The form also includes a list of information that is considered identifiable under the privacy rule regulations, and researchers are required to check off whether any of these will be obtained. ■

BEST PRACTICES SPOTLIGHT

IRB uses matrix to clarify research risks

Four harms by four degrees of risk

Evaluating research risk requires understanding a variety of potential harms and their nuanced impact. IRBs might find it useful to have a matrix to help explore each potential harm.

"In order to evaluate risk, you have to understand that it's a construction, a conceptual construction that we make where we try to get a sense of the severity of the harm," says **Paul Reitemeier**, PhD, chair of the human research review committee and associate professor of philosophy at Grand Valley State University in Allendale, MI.

"You have to identify the nature of the harm and its severity, and you have to identify the likelihood of it occurring," he adds.

Federal regulations identify four kinds of harm, so the IRB decided to look at four degrees of severity and four areas of harm. These form the rows and columns of the matrix.

"We decided to put an empirical descriptor in each box," Reitemeier says.

The four columns pertaining to the four levels of risk include potential harms of health/physical, privacy/social/legal, psychological, and financial. *(See information on these four potential harms, page 90.)*

Researchers find communicating risk to be a delicate dance, Reitemeier notes.

They want to provide adequate information without unnecessarily alarming potential subjects. The matrix with its empirical examples in each of the categories gives them a way to describe risk to participants and to better educate themselves about their study's risk, he adds.

The matrix doesn't address frequency because researchers often will not know a potential harm's frequency until the study is underway.

"You can imagine all kinds of research where the people who are asked to participate have a different understanding of what minimal or moderate or significant risk would mean," he says. "So the matrix is a tool to try to help the

researcher figure out how to describe a potential harm based on the type of harm and the severity of it," he explains.

An example of how differently scientists and a study population might view harm is what happened with the Havasupai Indians in Arizona over the past 24 years, Reitemeier says.

Researchers in 1990 obtained permission from the community to draw blood for research. Investigators initially hoped to learn more about the tribe's high rate of diabetes. But over the years, the blood samples were used for other genetic research, including study into the tribe's geographical origin.

"When they completed their research, they did a DNA analysis and determined these people came across the Bering Strait from Russia years ago," Reitemeier says. "This was upsetting to Native Americans because their culture said they had originated in the Grand Canyon."

Had the researcher or IRB anticipated this cultural and psychological harm, they could have provided better informed consent and took precautions to minimize the risk, he says.

The four rows of the matrix stipulating the severity of risk are these:

• **No more than minimal risk.** This is defined in the regulations as the risk you undertake if you are an average, normal, healthy person living in a safe environment, he says.

"It includes routine physical or psychological procedures or tests," he adds.

Blood tests and gathering information about height and weight are examples of no more than minimal risk.

• **Minor increase over minimal risk.** This one is ambiguously defined as more risk than minimal, but less than moderate, Reitemeier says.

• **Moderate risk.** "This is more harmful than most people would think about, but the harm has to be temporary," he explains. "It could last more than 24 hours, and it should be reversible with moderate discomfort, bodily function or pain."

Consider the risk associated with getting one's tooth drilled or if someone's private information is released with his or her identity attached and it appears to be socially embarrassing, he notes.

Consider psychological harm, defined subjectively, as upsetting, unwanted emotional responses, but not impairing, and they are transient.

"They go away after a while," Reitemeier says. "You might be sad and nervous and have your sleep disrupted, or it could be financial, a temporary or moderate financial cost or loss, a short absence from work where you lose wages, or it might be a waste of time if the research lacks scientific merit."

• **High risk and life-threatening risk.** "It is permissible for IRBs to review and approve research that carries that level of risk, but it has to have strong justification," Reitemeier says.

The matrix contains a series of examples of types of harm at different levels of risk. IRB reviewers can consult it when they're trying to make a determination, and IRB staff can use it when trying to decide if a study is exempt or requires an expedited or full board review, he explains. ■

Risk matrix contains four potential harms

Excerpts offer examples

The IRB at Grand Valley State University in Allendale, MI, uses a matrix that clarifies how IRB members and staff might describe various potential harms at four levels, from no more than minimal risk to high risk.

The five-page matrix further describes the classifications of risk, including these excerpts:

• **Health/physical harms.** "Medical research often involves exposure to minor pain, discomfort, or injury from invasive medical procedures, or harm from possible side effects of drugs. All of these should be considered 'risks' for purposes of IRB review."

• **Psychological harms.** "Stress and feelings of guilt or embarrassment may arise simply from thinking or talking about one's own behavior or attitudes on sensitive topics such as drug use, sexual preferences, selfishness, and violence. These feelings may be aroused when the subject is being interviewed or filling out a questionnaire. Stress may also be induced when the researchers manipulate the subjects' environment — as when 'emergencies' or fake 'assaults' are staged to observe how passersby respond. More frequently, however, is the possibility of psychological harm when behavioral research involves an element of deception."

• **Invasion of privacy.** "In the research context, it usually involves either covert observation or

'participant' observation of behavior that the subjects consider private."

"The IRB must make two determinations:

1. Is the invasion of privacy involved acceptable in light of the subjects' reasonable expectations of privacy in the situation under study; and

2. Is the research question of sufficient importance to justify the intrusion?"

• **Breach of confidentiality.** "Some research requires the use of a subject's hospital, school, or employment records. Access to such records for legitimate research purposes is generally acceptable, as long as the researcher protects the confidentiality of that information. However, it is important to recognize that a breach of confidentiality may result in psychological harm to individuals (in the form of embarrassment, guilt, stress, and so forth) or in social harm."

• **Social and economic harms.** "Some social and behavioral research may yield information about individuals that could 'label' or 'stigmatize' the subjects (e.g., as actual or potential delinquents or schizophrenics). Confidentiality safeguards must be strong in these instances.

"Participation in research may result in additional actual costs to individuals. Any anticipated costs to research participants should be described to prospective subjects during the consent process." ■

Out with the old IRB process, in with the new

Children's hospital adopts flexible model

For many years, the IRB office at Children's Hospital Los Angeles (CHLA) followed a process that was standard at most institutions: long, regularly scheduled meetings organized to review an ever-increasing number of protocols. "The approach of the human subjects protections program and the IRB had been the same for many years," says **Michele Kipke**, PhD, vice chair of research in the Department of Pediatrics at CHLA.

Feedback from the investigator community was mixed; researchers wanted a more streamlined process to accommodate the varied and expanding research program at CHLA, Kipke says.

"Knowing that we could improve this process, we defined some metrics that the staff tracked for several months," she says. The metrics included volume of administrative protocols, volume of full committee proposals, turnaround time, how quickly staff were moving a protocol along, how it was submitted, and how quickly division chiefs signed off. "We collected the data, and it was really informative," she says.

Kipke and colleagues learned that 75% of protocols received are expedited or administrative, yet turnaround time was on par with full committee reviews. The full reviews were much longer than the average turnaround time of other children's hospitals. "It told us that there was some work that we needed to do," Kipke says.

"In the early phase when we were monitoring turnaround time, we were seeing a lot of variability," she continues. "Measuring and looking at the data became an intervention in and of itself and helped to reduce turnaround times, but we hadn't put any specific interventions in place."

Flexible IRB

To cut down turnaround times and streamline the approval process, the office developed a flexible IRB model consisting of seven or eight core IRB committee members and a pool of 35 alternates. Meetings are now held once a week, and members from the pool of alternates can be called in as needed, usually when protocols call for a particular alternate's expertise. "This way, we have the right mix of expertise and knowledge base," Kipke says. "They are all scheduled, so there's no randomness to it and no one gets a call the day before, asking them to attend. We easily have a quorum and, by bringing in alternates, the right expertise is there to review." Members only have to attend one meeting per month.

The IRB has one chair and three vice chairs, with at least one present to facilitate each meeting. Meetings are typically limited to 90 minutes and have no more than six or seven protocols. "Another difference is that when you have a meeting with 35 committee members and 30 protocols, they're not looking at all 30 of them," she says. "They're only looking at the ones that interest them, or what they're assigned. Now with committee members assigned a smaller number of protocols, we believe the protocols are getting a more thorough review."

Pre-submission improvements

The team also clarified the expectations for

staff members and narrowed the pre-submission review process to make sure staff were not overreaching their responsibilities. "We created a checklist that they use for pre-submission review so they know they looked at everything they had to look at and that's all," Kipke says. "When they have a fully developed protocol, they can move that on and get the proposal seen within seven days of submission."

They also created a staff position dedicated to assisting investigators in developing and submitting protocols to ensure timely processing. The regulatory support specialist acts as a liaison between the study team and the IRB, educates and trains members of the study team on regulatory issues, assists with IRB application and submission, and assists with regulatory and compliance documentation and submission to study sponsors. "We've had fellows submitting protocols that weren't completed appropriately and were taking up a lot of time," Kipke says. "This new service helps investigators to submit a well-developed protocol."

They are also training certain IRB staff to handle administrative expedited reviews, protocol amendments, and other tasks that don't need to go to the chair or the full committee. "If you have an amendment to add staff to a protocol, there's no reason for that to go to the committee or chair," Kipke says. "That's something a well-trained staff member can review and sign off on."

"We did uncheck the Federal-wide Assurance box and we're now implementing changes associated with that," she continues. "For some of these reviews, like chart reviews, that are no-risk or studies with minimal to no risk, we're re-evaluating how often they need to come back for review. They had all been on annual review, which is not necessary for minimal-risk studies."

Tracking results

Since implementing the flexible IRB on January 1, Kipke says the improvements have been significant, and they are moving closer to the IRB's goal of 45 days average turnaround time. "I think we can do better than that, but that's been the goal from the start," she says.

"We're giving a short survey to every person who submits a protocol and gets it approved," she says. "We're six months into this now and everyone is feeling very positive about it." The survey data show an increasing number of investigators reporting a more positive experience with the flexible IRB, and overall they are very satisfied with the rationale given for protocol changes needed, guidance provided by the IRB, and support from the HSPP office.

They also plan to survey IRB members after six months to see if they have any recommendations. "The groups are running really well," Kipke says. "Each group has a rhythm and is getting protocols through really quickly and not sacrificing the integrity of the review. We report these numbers to the division chiefs and department chairs to show how we're doing and make this as open a process as possible."

Buy-in and training for staff was a little slow, Kipke says, but the goals are being accomplished. "There was a lot of training to be done for staff," she says. "The approach in the HSPP office and IRB had been the same way for many years, and there was work that needed to be done to help folks know what we're trying to achieve, and to lay out expectations. Change is hard, but we have a group that's still with us and working hard and committed, so we can declare success in that area as well."

"We're definitely at this point hitting goals we've set and achieving what we hoped to achieve," Kipke adds. ■

University system creates reliance service

UC hopes to serve as national model

Even as multicenter studies with central IRB reviews gain traction, some IRBs are still hesitant to join in. However, coordinating a multisite study among several IRBs within the same university system can be a time and paperwork hassle for both principal investigators and IRBs — and could make previously reluctant IRBs consider a new central reliance agreement.

Several years ago, the University of California system was conducting its multicampus National Institutes of Health studies with one overarching principal investigator or sub-PI at one of the campuses. All five academic medical centers would have the same NIH-funded project but had to get approval from all five IRBs, resulting in a major

time drain.

About eight years ago the directors of UC's academic medical centers got together to develop a memorandum of understanding (MOU), allowing multicampus research to be reviewed by only one IRB. "It was innovative at the time because there was — and, in a lot of cases, still is — reluctance among IRBs for relying on one institution," says **Eric Mah**, senior director of research compliance and interim Chief Ethics & Compliance Officer at UC San Francisco. "Fast forward to when BRAID began its project in 2012."

The University of California system created the UC Biomedical Research Accreditation, Integration, and Development (UC BRAID) program to increase research collaboration between the five UC campuses, speed multisite research approval, and reduce barriers to approval across the UC system.

"We discovered that dozens of studies were the same protocol, being reviewed by two or more IRBs," Mah says. "It [reliance] would save the investigators time, save the IRB time, and improve the site initiation time for every subsequent site. It would be a win-win for all."

Reliance Services

Such a reliance model requires serious support. "Critical to the success of this [program] was developing a service that could handle paperwork, processes, and the relationships between the other sites and the reviewing IRB," Mah says.

For example, Mah says, there may be a principal investigator (PI) at UC San Diego who submits a protocol to the UC San Francisco IRB, but this PI may not be experienced with the UC San Francisco IRB. Enter UC Reliance Services (UCRS), which can act as an interface between the UCSD PI and the UCSF IRB. "UC Reliance Services is kind of like a white-glove treatment concierge service," he says. "There are sometimes differences among sites; for example, different procedures that some sites follow and others don't, and modifications or protocol amendments that some sites follow and others don't. UC Reliance Services assists both the reviewing IRB and the PIs. Furthermore, IRB application submissions and post-approval forms are not always the same. The PI doesn't need to memorize five sets of forms for five potential reviewing IRBs; PIs and the IRBs have a service that helps everyone involved in the process."

UCRS is part of UC BRAID and was established to expand the use of UC MOU, eliminate duplicative IRB reviews, and provide centralized administrative support for industry-sponsored multicampus clinical trials.

UCRS looked at each campus's reliance processes and individual processes to develop standardized forms and communications. The office helps to reduce the administrative burden on PIs, research staff, and the local IRB offices. "[Reliance Services] also performs regular check-ins with sites to make sure things are going well," Mah says. "We also monitor continuing review and other modifications. Ideally, the local IRB doesn't experience additional workload. We've seen success in half a dozen studies at all five UC academic medical campuses."

Identifying potential multisite studies

Reliance Services also hopes in the near future to identify prospective researchers and studies for multicampus reliance. "One challenge is that not all five IRBs use the same electronic system," Mah says. "Some systems are homegrown, some are commercial systems. We are currently developing a tool where we can search for studies based on sponsors, protocol number, and study title to see whether the study had been approved or is currently undergoing review."

The system is a critical piece for identifying studies that can use central IRB reliance, Mah says. "Identifying potential studies and initiating the reliance at new campuses will be key to remaining competitive," he says. "Reliance Services also helps speed up site initiation. When the research community is small, they [researchers] know their colleagues are doing a study and they may want to do it, too."

Plans for phase two of the database development include prospectively identifying specific researchers at UC campuses. "For example, if a study is approved at UC San Francisco but not [UC] Davis, we could then turn to the database to find a PI in that [San Francisco] research area," Mah says. "We would ask if they can do the study, if they are available and interested. We can match studies in one catchment area to PIs in another, which can help CROs [contract research organizations] and study sites with recruitment and advance their patient subject recruitment in new ways. This can be the future of clinical research."

PIs have largely been satisfied with Reliance Services, Mah says. "I think there's a lot of appeal

when there's a service specifically devoted to helping them navigate the process," he says. "New site PIs don't have to submit a full IRB application, which is a huge time savings for them."

IRB trust

The campus IRBs have also been receptive, Mah says, partly due to trust and good relationships. "In many of these relationships, it's a matter of building trust and the notion that there may be some uncertainty, but they can trust and let go," he says. "We have worked together for a long time — I like to think we have good relationships among the campuses."

"I think there's a real sense of confidence in the review, primarily because it was coming from another academic medical center and those IRBs possess the expertise to review these studies, particularly the early-phase studies," he continues. "Unlike commercial IRBs — which may lack practicing physicians, or have physicians who are not active researchers — the majority of the academic medical center IRBs are clinicians and active researchers who have the expertise to review the really difficult studies."

So far, six studies have been approved using BRAID and UCRS. Approval time so far has been around two weeks, and getting the approval time down farther is a work in progress. "There were some bumps in the road — we engaged in a failed fast-forward model," Mah says. "It's okay to be inelegant at times and make mistakes and learn from them. We think we can get approval down to three to five days once it gets going. The current process [for submission and approval], unfortunately, is essentially manual with email and picking up the phone. Technology can help this process and automate it in some ways."

Other projects

The team at BRAID has also developed the University of California Research eXchange (UC ReX) program, a database that connects researchers to de-identified patient data from all five UC medical centers. The data helps researchers identify potential clinical trial subjects.

"I think it's an exciting time for our industry and it will change even more in the next five years," Mah says. "It's a pivotal time for us and hopefully the model we're using will be helpful to others. We hope that this could serve as a national model." ■

New ethics report for neuroscience research

"Be prepared to participate," expert says

The Presidential Commission for the Study of Bioethical Issues' May 2014 report, *Gray Matters: Integrative Approaches for Neuroscience, Ethics, and Society*, includes recommendations for institutions and individuals engaged in neuroscience research.

"Bioethicists should be prepared to participate in the integration of ethics and neuroscience," says **Lisa M. Lee**, PhD, MS, the Bioethics Commission's executive director.

Progress in contemporary neuroscience offers promise for discovering improved interventions, and perhaps cures, for neurological disorders that affect more than one billion people globally and millions of people in the United States, says Lee.

"A single ethical lapse in scientific research can cause a loss of public confidence, which can obstruct the progress of other research," she adds.

The report provides examples to illustrate important ethical issues relevant to neuroscience research. These are neuroimaging and brain privacy; dementia, personality, and changed preferences; cognitive enhancement and justice; and deep brain stimulation research.

"These examples highlight some of the ethical and societal issues that can arise in neuroscience research and the application of research findings," says Lee.

The Bioethics Commission recommended that institutions and individuals engaged in neuroscience research should:

- integrate ethics across the life of a research endeavor;
- identify the key ethical questions associated with their research;
- take immediate steps to make explicit their systems for addressing those questions;
- include substantive participation by persons with expertise in ethics on advisory and review panels.

"Many of these approaches necessitate direct involvement from bioethicists and other professionals with experience in ethics," says Lee.

"This volume is a short, high-level overview of the issues," says **Henry T. Greely**, JD, director of the Stanford Center for Law and the Biosciences

and chair of the steering committee at Stanford Center for Biomedical Ethics. "Its recommendations are good, and I hope they are followed. It really adds up to taking the ethical issues seriously."

The report's summary of the many ways in which ethics can be integrated into science may be quite useful, adds Greely. "Ethics are most important not for their effects on science, but on people," he says. "Consideration of ethical issues is needed to help make sure that people are safe and well-treated."

Anytime people think they have been harmed by scientific research or its results, or feel they have been lied to, cheated, or betrayed by researchers, is bad for science, says Greely. "The consequences of the Public Health Service's study of untreated syphilis among African-American men — the so-called Tuskegee study — still reverberate," he says.

There is a clear need, says Greely, to address questions of the safety, efficacy, and long-term personal and societal consequences of neuroscience-based predictions and interventions.

"Right now, issues of the ethics of research are foremost: questions of consent, confidentiality, incidental findings, and so on," says Greely. "But neuroscience is edging into clinical, consumer, educational, and even legal system use."

The report serves as an important symbolic gesture that ethics should be valued and prioritized, not only by those who conduct neuroscience research, but also by those who support the endeavor of neuroscience, says **Karen S. Rommelfanger**, PhD, neuroethics program director at Emory University in Atlanta.

"As noted in the report, often neuroscientists throughout their careers, as I have done at earlier points in my career as a neuroscientist, conflate ethics with compliance, and think of ethics narrowly as research ethics," she says.

Rommelfanger notes that the study of neuroscience, unlike many other scientific disciplines, "strikes at the core of who we think we are. Therefore, the ethical questions often move beyond research and professional ethics into the complex terrain of evaluating societal implications of our work."

These are the very questions that draw students and the public in to learn more about the brain. "This also means that neuroscientists have an enormous responsibility to be revisiting these questions in their own work as responsible stewards of their work," says Rommelfanger.

Neuroscientists must be afforded the time and resources to consider these questions, she says.

"The challenge ahead will be addressing how to implement these recommendations," says Rommelfanger, noting that the financial resources put forward for the BRAIN Initiative are still relatively modest, given the costs associated with conducting neuroscience research.

"Integrating ethics throughout the life of the research project will require a cultural change — starting with having resources that are clearly allocated to ethical inquiry," says Rommelfanger. ■

CNE/CME OBJECTIVES & INSTRUCTIONS

The CNE/CME objectives for *IRB Advisor* are to help physicians and nurses be able to:

- establish clinical trial programs using accepted ethical principles for human subject protection;
- apply the mandated regulatory safeguards for patient recruitment, follow-up and reporting of findings for human subject research;
- comply with the necessary educational requirements regarding informed consent and human subject research.

Physicians and nurses participate in this continuing education program and earn credit for this activity by following these instructions.

1. Read and study the activity, using the provided references for further research.
2. Scan the QR code below or log on to www.cmecity.com to take a post-test. First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice or renewal notice.
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the test, your browser will be automatically directed to the activity evaluation form, which you will submit online.
5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly. ■

COMING IN FUTURE MONTHS

- Controversy over Facebook mood study
- Handling variety of centralized IRB models is challenge
- Streamlined review solves big problems
- Serious adverse event reporting best practices

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CNE/CME QUESTIONS

1. Risk described as temporary and reversible with moderate discomfort, bodily function or pain would be labeled as which kind of potential harm, says Paul Reitemeier, PhD?
A. No more than minimal risk
B. Minor increase over minimal risk
C. Moderate risk
D. High risk and life-threatening risk

2. According to J. Bruce Smith, MD, CIP, a record/chart review/database research study template addressing HIPAA concerns might ask which of the following questions about how data will be used?
A. How many subject or database records will be reviewed?
B. Will data be sent outside of the institution?
C. How will data be sent?
D. All of the above

3. HIPAA rules were modified in early 2013 to allow which of the following?
A. Research sites have six additional identifiers to add to the list
B. Research sites are permitted to use a single authorization form for compound authorizations
C. Research sites must conduct a full HIPAA review for every study involving database work
D. All of the above

4. What is a function that UC Reliance Services does not perform, according to Eric Mah?
A. Acts as an interface between a PI and IRB
B. Performs regular check-ins with sites
C. Designs research protocols
D. Monitors continuing review